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14. ABSTRACT Using fMRI, we are conducting an observational study to characterize the pattern of brain activation during performance of cognitive control and working memory tasks in service personnel with mild traumatic brain injury (TBI) and severe TBI imaged between 3 and 42 months after injury. To date, 447 patients with TBI at Walter Reed Army Medical Center (WRAMC) have been screened. Thirteen patients diagnosed with TBI, resulting from blast, have met eligibility criteria and enrolled in the protocol. Nine patients have completed the neuropsychological testing and four have completed subsequent MRI series. National Naval Medical Center (NNMC) has been added as a research site to address the unexpectedly low rate of eligible patients at WRAMC and consequent slow recruitment into the protocol. NNMC IRB gave final approval of the protocol 13 October 2010. Continuing review reports are in place at WRAMC, NMRC, and NNMC. Continuation was approved by WRAMC on 14 December and NNMC IRB will meet on 10 February for review. Contributions from the present study, specifically the addition of a patient group with severe TBI associated with blast, are expected to complement research findings with this patient population recently released and upcoming in the literature (Levin et al., 2010; Brody et al., under review).				
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INTRODUCTION:

Blast-related traumatic brain injury (TBI) is sparsely documented in the present medical research literature. Given the complex patterns of axonal injury believed to underlie blast specific injury, a reliance on conventional neuroimaging techniques may be partly responsible for this deficiency. Novel brain imaging techniques provide promise for increasing neuroimaging sensitivity in this patient population. Specifically, functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) represent opportunities for enhancing utility of imaging in the study of blast-related TBI, potentially leading to improvement in rehabilitation therapies. Using these imaging modalities, we are conducting a dual cohort study to characterize the pattern of brain activation during performance of cognitive control and working memory tasks in service personnel with mild and severe TBI imaged between 3 and 42 months post injury. Findings in this work will augment those of Dr. Harvey Levin whose work is the model for this protocol [e.g., Levin, H. S. et al. (2010). Diffusion tensor imaging of mild to moderate blast-related traumatic brain injury and its sequelae. Journal of Neurotrauma, 27, 683-694.]

BODY:

To date, 447 Walter Reed Army Medical Center (WRAMC) TBI patients have been screened for eligibility in this protocol. Patients who did not meet the eligibility criteria were most frequently excluded due to non-blast related causes of TBI diagnosis (e.g., motor vehicle accident or blunt force trauma). Of patients screened, 66 met all protocol eligibility criteria. 30 eligible patients declined to participate, and 21 were not approached for various reasons (e.g., request by Case Manager not to approach). Thirteen eligible patients have enrolled in the protocol. Nine patients have completed the neurological testing. Four patients have completed the MRI series. One patient has completed the 3- and 6-month telephone follow-up interviews, thereby concluding that patient's enrollment in the study.

Patient recruiting is ongoing. The description of eligible and enrolled patients to date remains consistent with the previous reports from.

Progress towards goals described in statement of work:

- The National Naval Medical Center (NNMC) was added to the protocol as an additional recruitment site. CDR Forest Sheppard, MC USN (surgeon) and Dr. David Williamson (neuropsychiatrist) are NNMC collaborators for this protocol. NNMC granted approval on 13 October 2010. (The protocol amendment to add NNMC as a site was approved by WRAMC IRB 25 August 2010.) The amended

- WRAMC protocol and the NMRC protocol were approved by CDMRP on 24 November 2010. The supporting NIH protocol was renewed on 7 December 2010. The protocol is currently actively recruiting participants.
- Continuing review reports were submitted to WRAMC, NNMC, NMRC, and CDMRP. The review was approved by WRAMC on 14 December, and by NNMC and NMRC on 10 February.
 - A request for a no-cost extension of the protocol was submitted to CDMRP.
 - A presentation of the protocol methodology and abbreviated findings was presented at the DOD TBI Imaging in Progress Review on 31 January 2011.

Problems encountered:

- The availability of MRI scanner time at NIH will be significantly reduced in the spring of 2011. NIH has announced the retirement of the NMRF3T MRI scanner. The scanner will be taken off line in March of 2011 and replaced. NIH has indicated that the process will require several months, during which users will be required to find arrangements to use scan time on other NIH scanners. In order to avoid down time, likely to result from reduced scan time availability, we have transitioned the study to a comparable MRI scanner in the NIH department of radiology.
- Patient recruitment at WRAMC continues to be impeded by low volume of eligible participants and high number of research protocols recruiting patients with TBI. The addition of NNMC as a patient recruitment site is intended to address this issue.
- MRI safety criteria at NIH include specification of manufacturer for surgical hardware installed (e.g., fixators). Product manufacturer information was found for all enrolled patients. One manufacturer could not verify MRI safety. As a result, two patients were terminated from the protocol for MRI safety considerations, per NIH safety policy.

KEY RESEARCH ACCOMPLISHMENTS:

- The study was successfully transitioned to an alternate MRI scanner in order to avoid likely down time which was expected to occur in March, due to the retirement of the MRI scanner previously used by the study.
- MRI series from the most recently enrolled patient were collected on the transitioned Siemens 3T scanner.
- This protocol is the first approved research protocol at the National Intrepid Center of Excellence (NICoE).

REPORTABLE OUTCOMES

There are currently too few data points to produce a meaningful analysis.

CONCLUSION

The research by our study partner, Dr. Harvey Levin, closed without being able to include a more severely injured patient group in the sample (as was the original design). Reporting to date (Levin et al., 2010), suggests minimal benefit of DTI procedures. Other research with this diagnostic category, but more severely injured and evaluated closer in time to point of injury, suggests the contrary [Brody et al., under review, described via personal communication June 2010 and August 2010 (NNS and ATACCC meetings, respectively)]. As an extension of Dr. Levin's successful research model, we anticipate that the contributions from our present study, specifically the addition of a patient group with severe TBI associated with blast, will complement and augment research findings to date.